INFORMED CONSENT

TITLE OF RESEARCH: **RAD 1801/UAB 1803 – Pilot Study of Intra-Urethral Radiotransponder Beacon Guided Focal Prostate Stereotactic Body Radiotherapy**

IRB PROTOCOL NUMBER: **IRB-300002183**

SPONSOR: **Varian Medical Systems**

SPONSOR PROTOCOL NO.: **RAD 1801/UAB 1803**

PRINCIPAL INVESTIGATOR: **Andrew M. McDonald, MD, MS**

CO-INVESTIGATORS: **Soroush Rais-Bahrami, MD; John Fiveash, MD; Michael Dobelbower, MD, PhD; Rojymon Jacob, MD; Robert Kim, MD; Eddy Yang, MD, PhD; Richard Popple, PhD; Rex Cardan, PhD; Ivan Brezovich, PhD; Jeffrey Nix, MD**

General Information	You are being asked to take part in a research study. This research study is voluntary, meaning you do not have to take part in it. The procedures, risks, and benefits are fully described further in the consent form.
Purpose	The purpose of this study is to confirm that treatment to part of the prostate gland (focal treatment) is feasible using stereotactic body radiotherapy (SBRT) with real time guidance by intra-urethral radiotransponder beacons.
Duration & Visits	You will receive 5 treatments over a 9-17 day period. You will be asked to visit your study doctoror visit will be conducted remotely, if necessary, after your treatment is completed every 3 months for the first year, then every 6 months for year 2. After year 2, your study doctor will continue to monitor your prostate cancer as part of your routine cancer care.
Overview of Procedures	If you decide to take part in the study, you will have a urinary catheter, with radiotransponder beacons inside, placed before undergoing stereotactic body radiotherapy (SBRT). The radiotransponder beacons will guide the accuracy of your treatment. You will receive 5 treatments over a 9-17 day period. Over the course of the study, you will undergo evaluation of your ability to carry out daily activities, routine blood draws (including PSA levels), MRI scans, biopsy of the prostate, completion of quality of life questionnaires, and evaluation of any side effects you may be having.
Risks	The main risk of participation in this study is that compared to other treatments, your prostate cancer may be more likely to come back after this treatment. The most common risks are loose stools, decrease in overall erectile function, urinary retention, and hemorrhoid irritation or minimal rectal bleeding.
Benefits	You may or may not benefit directly from taking part in this study. A possible benefit includes fewer side effects compared to men who have radiation

	therapy to their entire prostate gland. Personal benefit may not result from taking part in this study, but knowledge may be gained that will benefit others.
Alternatives	The alternatives to you participating in this study are: • Getting treatment or care for your cancer without being in the study • Taking part in another study • Getting no treatment

INTRODUCTION

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have early stage prostate cancer and you have elected to receive radiation therapy.

PURPOSE OF THE STUDY

Traditional prostate cancer therapies include surgical removal of the entire prostate (prostatectomy) or standard radiation treatment to the whole prostate gland. Currently, men who are diagnosed with low or low-intermediate risk prostate cancer must choose between active surveillance ("watchful waiting") or whole prostate treatment, which can additional side effects. Focal treatment is to target the area of the prostate that contains the most cancer rather than treating the entire prostate gland. Focal treatment for prostate cancer may offer an ability to reduce the amount of damage to the entire prostate gland and surrounding areas while still treating the cancer effectively.

Stereotactic body radiotherapy is a type of radiation treatment that gives fewer but higher doses of radiation than standard radiation. It uses special equipment to position the patient and guide focused beam toward the cancer and away from normal surrounding prostate tissue. The higher dose technique may work better to kill cancer cell potentially with fewer side effects than standard radiation therapy.

In this study, you will receive focal prostate stereotactic body radiotherapy (SBRT). You will receive five total treatments, spaced out over a 9-17 days period. To help guide the accuracy of the treatment, a urinary catheter, which contains 3 radiotransponder beacons, will be inserted before each treatment. Radiotransponder beacons are tiny seeds, about the size of a grain of rice, that send out radio waves to tell the radiation therapy machine where to aim. This lets the machine adjust for movements and may allow less radiation to go to normal tissues

The purpose of this study is to assess the feasibility of focal prostate stereotactic body radiotherapy (SBRT) with real time guidance by intra-urethral radiotransponder beacons for men with low and low-intermediate risk prostate cancer. This type of study is called a pilot trial. This means that the main goal of the study is to confirm that the technique is possible to use. We plan to enroll 10 patients to this study.

EXPLANATION OF PROCEDURES

Before you begin the study

You will need to have the following exams, tests, or procedures to find out if you can be in the study. Most of these exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor. Some of these study procedures may be conducted remotely, if necessary.

- Complete medical history and physical exam, including a digital rectal exam (DRE).
- A blood test to determine your PSA (a value that helps determine the stage of your prostate cancer). About 2 teaspoons of blood will be drawn from a vein and processed in the lab.
- A CT scan with a urinary catheter will be utilized for planning the radiation. A local anesthetic will be used prior to insertion of the catheter to reduce pain and/or discomfort.
- MRI (Magnetic Resonance Imaging)/MRS of the prostate, likely without contrast.
- Research Requirement: You will be asked to fill out a questionnaire on urinary symptoms and function called the American Urological Association Symptom Index (AUA SI).
- Research Requirement: You will be asked to fill out a questionnaire on sexual health called Sexual Health Inventory for Men (SHIM).
- Research Requirement: You will be asked to complete a questionnaire: the Expanded Prostate Index Composite (EPIC). The EPIC assesses bowel, urinary, and sexual function. It takes about 15 minutes to complete. Completion of the EPIC is mandatory for this study.

Treatment

You will receive 5 radiation treatments to the prostate during this study. The treatments will be spaced out over a 9-17 day period. For each treatment, you will come to the UAB Department of Radiation Oncology clinic and we will place a urinary catheter into your penis. Three radiotransponder beacons will be inside the urinary catheter. Radiotransponder beacons are tiny seeds, about the size of a grain of rice, that send out radio waves to tell the radiation therapy machine where to aim. This lets the machine adjust for movements and may allow less radiation to go to normal tissues. Once the catheter has been placed, you will be taken to the treatment room and asked to lie down on the table. You will lie on the table for about 30 minutes while your doctors take x-rays, check the radiotransponder beacons, and then administer the radiation. Once the treatment is over, we will remove the urinary catheter, along with the radiotransponder beacons, and you will be able to leave.

You will be asked to fill out an American Urological Association Symptom Index (AUA SI) questionnaire on the last day of treatment.

After Treatment

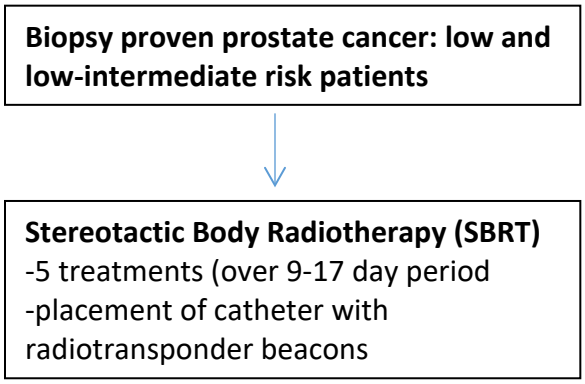
You will need these tests and procedures every 3 months for the first year following the start of radiation, every 6 months for year 2. Some of these study procedures may be conducted remotely, if necessary.

- A blood test to determine your PSA (a value that helps determine the stage of your prostate cancer).
- Assessment of any side effects you may be experiencing from the treatment.
- Research Requirement: You will be asked to complete an American Urological Association Symptom Index (AUA SI) and Sexual Health Inventory for Men (SHIM) questionnaires and the Expanded Prostate Index Composite (EPIC). The EPIC assessed bowel, urinary, and sexual function. It takes about 15 minutes to complete. Completion of each questionnaire is mandatory for this study.

An MRI and targeted biopsy of your prostate gland will be performed 1 year from the completion of radiation. This is a standard procedure for patients who undergo focal treatment for prostate cancer.

Study Plan

Another way to find out what will take place during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



LENGTH OF STUDY

You will receive a total of 5 treatments over a 9-17 day period. After you are finished receiving radiation, the study doctor will ask you to visit the office (or will be conducted remotely) for follow-up exams every 3 months for the first year, then every 6 months for year 2. After year 2, your doctor will continue to monitor your prostate cancer as part of your routine cancer care.

RISKS AND DISCOMFORTS

The main risk of this study is that treatment of only part of the prostate gland may increase the risk that your prostate cancer recurs or progresses after the treatment. Researchers do not know how much more likely it is that your prostate cancer may return with this study treatment compared to other treatments.

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the treatment. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to the radiation include:

Likely

- An increase in urinary frequency, i.e., having to urinate more often
- An increase in the amount of times you urinate at night
- A decrease in strength of urine stream flow
- An increase in bowel movement frequency
- Loose stools
- Decrease in overall erectile function if good baseline function is present

Less Likely

- Hemorrhoid irritation or minimal rectal bleeding
- Urinary retention requiring catheterization
- Rectal, bladder, or prostate discomfort requiring narcotic medications
- Urinary bleeding requiring intervention or blood transfusion
- Nausea
- Small amount of urinary bleeding
- Loss of erectile function if good baseline function present
- Inability to pass urine requiring temporary or one-time urinary catheter

Rare but Serious

- Small bowel scarring causing small bowl obstruction
- Small risk of developing a cancer from exposure of normal tissues to radiation
- Rectal bleeding (greater than that encountered from hemorrhoid flares)
- Rectal bleeding requiring surgical repair or blood transfusion
- Inability to pass urine requiring a medical procedure intervention other than catheterization
- A new malignancy caused from CT scan radiation or radiation used for treatment (less than 2% chance)

Risks and side effects related to placement of urinary catheter:
As part of this study, you will have a urinary catheter placed and removed a total of 6 times. Placement of a urinary catheter is associated with discomfort and there is a potential for the amount of discomfort to increase with each subsequent placement, due irritation of your urethra from the catheter and from the radiation treatment. If you experience pain from the catheter, then your doctor will talk to you about medication that can help reduce the pain.

Placement of a urinary catheter has also been shown to increase your risk for developing a urinary tract infection.

Risks and side effects related to MRI:
The administration of a MRI is standard of care for many patients with prostate cancer. MRI contains no ionizing radiation. To date, there have been no documented significant side effects of the magnetic fields and radio waves used on the human body. We do not anticipate regular IV gadolinium contrast to be utilized on this protocol for MRI or MRS scans. Standard of care precautions, including careful attention to patient risk factors from MRI events will be taken.

MRI is a low-risk imaging procedure for most patients. However, if you have any of the following conditions, the exam may be dangerous for you. Please let the research staff know if you have any of these conditions:

- Implanted medical device (pacemaker, hip implant, surgical clips or shunts, artificial heart valve set, IUD, etc.)
- Hearing aid
- Body piercing
- Metal fragments (such as bullets) inside the body

Standard UAB MRI precautions will be taken for all patients, and no MRI's will be administered to patients that do not meet UAB standards for MRI safety.

Risks and side effects related to MRI with contrast:
MRI contains no ionizing radiation. To date, there have been no documented significant side effects of the magnetic fields and radiowaves used on the human body. You will be placed inside a scanner and asked to lie still for approximately 30 minutes to 1 hour. This is a noisy exam; you will be given earplugs to protect your hearing. To prepare the patient for their MRI exam, a liquid called a "contrast dye" will be injected into your veins to improve the quality of the image. There is a small possibility that you could have a severe allergic

reaction to this dye that could cause injury or death. If you have any kidney problems, the dye may cause other medical problems. If you have any kidney problems or have ever had allergic reactions to contrast dye, you must let the study physician know as soon as possible.

Information for Men Capable of Fathering a Child
There is a risk of not being able to father children in the future. If you think you may want to have children in the future, discuss this with the study doctor. Cryopreservation of sperm is not a part of this study. Discuss this option with Dr. McDonald and his associates.

For more information about risks and side effects, ask your study doctor. The location of your tumor may predict your risk of some side effects.

BENEFITS

You may or may not benefit directly from taking part in this study. A possible benefit includes fewer side effects compared to men who have radiation therapy to their entire prostate gland. Personal benefit may not result from taking part in this study, but knowledge may be gained that will benefit others.

SIGNIFICANT NEW FINDINGS

You will be told by your doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

ALTERNATIVE TREATMENTS

Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment

Your doctor can provide detailed information about your disease and the benefits of the various treatments available. You should feel free to discuss your disease and your prognosis with the doctor. The physician involved in your care will be available to answer any questions you may have concerning this program.

Talk to your study doctor about your choices before you decide if you will take part in this study.

CONFIDENTIALITY AND AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What protected health information may be used and/or given to others?
All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of any kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills; any other information related to or collected for use in the research study, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes; records about any study drug you received or about study devices used; and consent forms from past studies that might be in your medical record.

Your consent form will be placed in your medical record at UAB Health System. This may include either a paper medical record or electronic medical record (EMR). An EMR is an electronic version of a paper medical record of your care within this health system. Your EMR may indicate that you are on a clinical trial and provide the name and contact information for the principal investigator.

If you are receiving care or have received care within this health system (outpatient or inpatient), results of research tests or procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing medical record.

If you have never received care within this health system (outpatient or inpatient), a medical record will be created for you to maintain results of research tests or procedures.

Results of research tests or procedures may be placed in your medical record. All information within your medical record can be viewed by individuals authorized to access the record.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Who may use and give out information about you?
Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?
All Individuals/entities listed in the informed consent document(s), including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere). Your information may also be given to the sponsor of this research. “Sponsor” includes any persons or companies

that are working for or with the sponsor, or are owned by the sponsor, or are providing support to the sponsor (e.g., contract research organization).

Information about you and your health which might identify you may be given to:

- the Office for Human Research Protections (OHRP)
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- the University of Alabama at Birmingham - the physicians, nurses and staff working on the research study (whether at UAB or elsewhere); other operating units of UAB, UAB Hospital, UAB Highlands Hospital, University of Alabama Health Services Foundation, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the UAB IRB and its staff
- the billing offices of UAB and UAB Health Systems affiliates and/or Children's of Alabama and its billing agents

Why will this information be used and/or given to others?
Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. In addition, people from the sponsor and its consultants will be visiting the research site. They will follow how the study is done, and they will be reviewing your information for this purpose.

The UAB Data and Safety Monitoring Board maintained by the UAB Comprehensive Cancer Center will be meeting regularly to monitor safety and other data related to all active protocols (Phase I, II, and III). The Board members may receive confidential patient information, but they will not receive your name or other information that would allow them to identify you by name.

Information obtained during the course of the study which, in the opinion of the investigator(s), suggests that you may be at significant risk of harm to yourself or others will be reportable to a third party in the interest of protecting the rights and welfare of those at potential risk.

What if I decide not to give permission to use and give out my health information?
By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?
You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically. The use of your personal health information will continue until you cancel your permission.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?
If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others. Including others outside of UAB, without your permission.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this study at any time. Your choice to leave the study will not affect your relationship with this institution. However, you should return to see the study doctor for safety reasons so you can be taken off the study and referred for follow-up care. Contact the study doctor if you want to withdraw from the study.

You may be removed from the study without your consent if the study doctor decides it is not in the best interest of your health or if you are not following the study rules.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

COSTS OF PARTICIPATION

The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

PAYMENT FOR PARTICIPATION

You will not be paid for taking part in the study.

PAYMENTS FOR RESEARCH RELATED INJURIES

UAB and Varian Medical Systems have not provided any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be free of charge.

QUESTIONS

If you have any questions, concerns, or complaints about the research or a research-related injury, please notify Dr. Andrew McDonald, the Principal Investigator, at UAB Department of Radiation Oncology, (205) 996-5669. For more information concerning any of the procedures, you may contact the Research Nurse Coordinators at (205) 975-2880 or 978-2848 at the UAB Department of Radiation Oncology.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday.

LEGAL RIGHTS

You are not waiving any of your legal rights by signing this informed consent document.

SIGNATURES

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____ _____

Signature of Participant Date

_____ _____

Signature of Investigator or Person Obtaining Consent Date